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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,598	01/24/2002	Joseph A. Sorge	25436/2132	4699

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EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 08/26/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,598	SORGE ET AL.	
	Examin r	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1054* is/are pending in the application.

4a) Of the above claim(s) *30-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-29 in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 30-54 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1-29 are addressed below.

Specification

2. The disclosure is objected to because of the following informalities:

(a) The use of the trademarks "Taqman", "Scorpions", "Sunrise" (see pages 2),"Texas Red", "Lissamine", "Oregon Green", "Cascade Blue" (see page 36) and "QIAquick" (see page 54) have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

(b) The specification contains brackets at pages 20, 33, 34 and 38 not intended to encompass an amendment (see 37 CFR 1.121 (e)(2)(ii)). It is suggested removing the brackets from the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 12, 13 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Kwok et al (US 5,945,283, *patent date: August 31, 1999*). Regarding claims 12 and 26, Kwok et al. teach a composition and kit for identifying a target nucleotide sequence in a sample, the composition and kit comprising an oligonucleotide sequence comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of the target sequence, and is covalently attached to a tag molecule; and an anti-tag molecule which binds to said tag molecule, said anti-tag molecule labeled with a first member of a pair of interactive labels (column 3, lines 46-57). In the kit, Kwok et al. further teach packaging materials thereof (column 10, lines 15-25).

Regarding claim 13, Kwok et al discloses the composition of claim 12, wherein the tag is located on the 5' terminal of said oligonucleotide primer (see figure 1). Therefore, Kwok et al. meets the limitations of claims 12, 13 and 26.

5. Claims 1, 17, 19 are rejected under 35 U.S.C 102(a) and 35 U.S.C. 102(e) as being anticipated by Nadeau et al. (US 6,316, 2000 B1, *Patent date: November 13, 2001 for the 35*

U.S.C. 102(a) rejection and filing date: June 8, 2000 for the 35 U.S.C. 102(e) rejection). Regarding claim 1, Nadeau teach a composition for identifying a target sequence in a sample, the composition comprising (a) an oligonucleotide primer comprising a sequence which hybridizes to a complementary sequence 3' of the target nucleic acid and a second sequence which does not hybridize to said target polynucleotide in the presence of a third sequence; and (b) an oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide, said oligonucleotide probe labeled with a first member of a pair of interactive labels (column 4, lines 51-67 to col. 5, lines 1-5).

Regarding claim 17, Nadeau et al teach the composition of claim 1, wherein the second sequence is at the 5' end of said first sequence (column 4, lines 53-55).

Regarding claim 19, Nadeau et al teach the composition of claim 1, wherein one member of the pair of interactive labels is a quencher molecule (col. 4, lines 64-67). Therefore Nadeau et al. meets the limitations of claims 1, 17 and 19 of the instant invention.

6. Claims 1, 12-16, 20 and 26-29 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as being anticipated by Huang et al (US 6,287,778 B1, *patent date: September 11, 2001 for the 35 U.S.C. 102(a) rejection and filing date: October 19, 1999 for the 35 U.S.C. 102(e) rejection*).

Regarding claims 1 and 20, Huang et al. teach a composition and kit for the identification of nucleotides at a predetermined position in a nucleic acid sample, the composition and kit comprising an oligonucleotide sequence comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of the target nucleic acid sequence and a second sequence located at the 5' end which does not hybridize to said target in the presence of a third sequence;

and an oligonucleotide probe comprising said third sequence which hybridizes to said seconds sequence of said oligonucleotide sequence, said oligonucleotide probe labeled with a first member of a pair of interactive labels. The reference further teaches packaging material therein for the kit (col. 6, lines 9-28; see also column 9, lines 64-67 to col. 10, lines 1-2 and col. 16, lines 50-60).

Regarding claims 12, 13 and 26, a compositions and kit for the identification of nucleotides at a predetermined position in a nucleic acid sample, the composition and kit comprising an oligonucleotide comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of target nucleic acid and is covalently attached to a tag molecule at the 5 end of the oligonucleotide sequence, and an anti-tag molecule which binds to said tag molecule, said anti-tag molecule labeled with a first member of a pair of interactive labels. Huang et al. further teach packaging material thereof for use with the kit (Col. 6, lines 9-28; see also col. 9, lines 17-22 and col. 16, lines 50-62).

Regarding claims 14-16 and 27-29, Huang et al. disclose the composition and kit of claims 12 and 26, wherein said tag molecule may comprise a first member of a specific binding pair and wherein said anti-tag molecule may comprises the second member of a specific binding pair, wherein said specific binding pair is a biotin-streptavidin pair (page 16, column 50-58 and col. 17, lines 9-12 and lines 15-19). Therefore, claims 1, 14-16, 20 and 26-29 are anticipated by the reference of Huang et al.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 2-6, 8-11, and 21-24 rejected under 35 U.S.C. 103(a) as being unpatentable over Nadeau et al. (US 6,316,200 B1) as applied to claims 1, 17 and 19 above in view of Goelet et al. (US 5,888,819, March 1999). Regarding claims 2-6, 11, 18, 21-24, Nadeau et al teach a composition comprising for detecting a target nucleotide sequence in a sample, the composition comprising an oligonucleotide sequence which hybridizes to said target polynucleotide immediately 3' of the target sequence, a second sequence which does not hybridize to said target polynucleotide in presence of a third sequence; and oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide sequence, said oligonucleotide probe labeled with a first member of a pair of interactive labels. Nadeau et al differs from the instant invention in that the reference does not teach wherein a polynucleotide

terminator is incorporated into the composition or wherein the polynucleotide terminator comprises a member of a pair of interactive labels.

Goelet et al teach a composition and kit comprising an oligonucleotide primer comprising a sequence which hybridizes to said target polynucleotide immediately 3' of a target nucleotide sequence and a first, second third and fourth polynucleotide terminator that are not identical, which is incorporated in a template-dependent manner into said oligonucleotide primer by a polynucleotide synthesis enzyme (col. 4, lines 62-67 to col. 5, lines 1-20, 38-52). Goelet et al further teach wherein the first, second, third and fourth polynucleotide terminator are label with a detectable marker, wherein the detectable marker may be a fluorophore or a moiety to which an isotopically labeled moiety such as e.g., a fluorophore can be attached. Goelet et al further teach that using all four terminators comprising different detectable markers ensures fidelity, i.e., suppression of misreading. The authors continue by stating that by specifically labeling one or more of the terminators, the sequence of the sequence of the extended primer can be deduced and moreover, more than one reaction product can be analyzed per reaction if more than one terminator is specifically labeled (col. 15, lines 8-14). Goelet et al differ from the instant invention in that the reference does not teach wherein the detectable marker of the polynucleotide terminators comprise a pair of interactive labels which interact with each other to generate a signal by fluorescent resonance energy transfer.

In a method similar to that of Nadeau et al and Goelet et al for detecting a target nucleotide sequence, Kwok et al. teach a composition and kit comprising an oligonucleotide sequence comprising a first sequence which hybridizes to the target polynucleotide immediately 3' of the target sequence, and is covalently attached to a tag molecule; and an anti-tag molecule

which binds to said tag molecule, said anti-tag molecule labeled with a first member of a pair of interactive labels (column 3, lines 46-57). Kwok et al further teach wherein the composition comprises a first, second, third and/or fourth polynucleotide terminator labeled with a first member of a pair of interactive label which interacts with a second member of a pair of interactive labels to generate a signal by fluorescent resonance energy transfer (col. 3, lines 46-57, col. 5, lines 15-28 and lines 57-60; see also column 7, lines 42-50). Kwok et al teach that the composition comprising polynucleotide terminators labeled with a pair of interactive labels for use in methods of detecting a target polynucleotide sequence is advantageous because it allows the detection of a target nucleotide sequence to be accomplished in one reaction vessel without the requirement for separation or purification steps.

Therefore in view of the foregoing, one of ordinary skill the art at the time of the claimed invention would have been motivated to have modified the composition for detecting a target nucleotide as taught by Nadeau et al. in view of Goelet et al to further comprise polynucleotide terminators labeled with a pair of interactive labels which generate a signal by fluorescent resonance energy transfer. One of ordinary skill in the art would have been motivated to do so for the advantages taught by Kwok et al that a composition comprising polynucleotide terminators labeled with a pair of interactive labels for use in methods of detecting a target polynucleotide sequence is advantageous because it allows the detection of a target nucleotide sequence to be accomplished in one reaction vessel without the requirement for separation or purification steps.

Regarding claims 8-10, Goelet et al. wherein said oligonucleotide comprises a separation moiety that permits separation of said oligonucleotide primer and wherein said composition

further comprises a target moiety specific for said separation moiety, wherein separation moiety binds to said target moiety to permit said separation. Goelet et al additionally teach wherein said target moiety is attached to a solid support (col. 12, lines 44-56).

10. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nadeau et al. as previously applied above in view of Soderlund et al (US 6,013,431, January 11, 2000). Regarding claim 18, Nadeau et al teach a composition comprising for detecting a target nucleotide sequence in a sample, the composition comprising an oligonucleotide sequence which hybridizes to said target polynucleotide immediately 3' of the target sequence, a second sequence which does not hybridize to said target polynucleotide in presence of a third sequence; and oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide sequence, said oligonucleotide probe labeled with a first member of a pair of interactive labels. Nadeau further teach wherein the composition comprises four non-labeled conventional deoxynucleotides. Nadeau et al differs from the instant invention in that the reference does not teach wherein the composition further comprises a labeled conventional deoxynucleotide, and three other unlabeled chain terminators, wherein said labeled conventional deoxynucleotide is incorporated into the oligonucleotide primer at a position corresponding to the predetermined nucleotide of the target in a sample.

Soderlund et al teach a composition for detecting a nucleotide at a predetermined position in a target polynucleotide, the composition comprising a oligonucleotide primer that comprising a sequence immediately adjacent to the target nucleotide at the 3' end and one or more conventional deoxynucleotides incorporated into the oliogonucleotide primer, and optionally

unlabeled chain terminators corresponding to the other three nucleotide residues (col. 3, lines 49-66). Soderlund et al teach that the use of a labeled deoxynucleotide which corresponds to the variable nucleotide allows for specific point mutations to be detected (col. 8, lines 31-52). Soderlund et al further teach that the addition of chain terminators are advantageous because they provide a means for preventing incorporation of possible remaining conventional deoxynucleotides from the modification step (col. 8, lines 49-57). Soderlund et al that the modification step comprise modification of the oligonucleotide primer to include attachment moieties (any component which having affinity for another component forms an affinity pair with that other component (col. 5 beginning at line 24 to col. 6, line 18).

Therefore, in view of the foregoing, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to have modified the composition of Nadeau et al. with the composition of Soderlund et al to further incorporate a labeled conventional deoxynucleotide and three other labeled chain terminators. One of ordinary skill in the art would have been motivated to modify the composition as such for the advantages taught by Soderlund that the use of a labeled deoxynucleotide which corresponds to the variable nucleotide allows for specific point mutations to be detected and the addition of chain terminators provide a means for preventing incorporation of possible remaining conventional deoxynucleotides from the modification step.

11. Claims 7 and 25 rejected under 35 U.S.C. 103(a) as being unpatentable over Nadeau et al in view of Goelet et al as previously applied and further in view of Sorge et al. (WO 01/32887 A1, May 10, 2001). Regarding claims 7 and 25, Nadeau et al. in view of Goelet et al teach a

composition for identifying a nucleotide at a predetermined position of a target polynucleotide, said composition comprising an oligonucleotide sequence which hybridizes to said target polynucleotide immediately 3' of the target sequence, a second sequence which does not hybridize to said target polynucleotide in presence of a third sequence; and oligonucleotide probe comprising said third sequence which hybridizes to said second sequence of said oligonucleotide sequence, said oligonucleotide probe labeled with a first member of a pair of interactive labels, and wherein the composition further comprises one or more polynucleotide terminators incorporated in a template-dependent manner by a polynucleotide synthesis enzyme. The reference of Nadeau et al in view of Goelet et al differs from the instant invention in that the reference do not teach wherein the polynucleotide synthesis enzyme is a JDF-3 DNA polymerase.

In a general teaching, Sorge et al discloses a JDF-3 DNA polymerase and the use of the JDF-3 DNA polymerase in a template-dependent synthesis reaction. Sorge et al teach that a JDf-3 DNA polymerase has reduced discrimination (the tendency of DNA polymerase to not incorporate non-conventional nucleotides into a nascent DNA polymer) against a non-convention nucleotide such at dideoxynucleotides, ribonucleotides and conjugated nucleotides (page 9, lines 19, 20, page 10, lines 22-24, pages 13-15).

Therefore, in view of the foregoing one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the composition as taught by Nadeau et al. and Goelet et al to incorporate a polynucleotide synthesis enzyme such as a JDF-3 DNA polymerase instead of the standard DNA-dependent polymerases as described by Nadeau et al and Goelet et al for the advantages taught by Sorge et al a JDf-3 DNA polymerase has

reduced discrimination (the tendency of DNA polymerase to not incorporate non-conventional nucleotides into a nascent DNA polymer) against a non-convention nucleotide such at dideoxynucleotides, ribonucleotides and conjugated nucleotides.

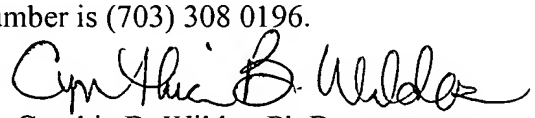
Conclusion

12. No claims are allowed

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm and on Friday from 9:30 am to 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308 0196.



Cynthia B. Wilder, Ph.D.
Examiner
Art Unit 1637

cbw